

TOBACCO INDUSTRY RESEARCH COMMITTEE

150 East Forty Second Street New York 17, New York

Application for Research Grant

#238

Date: May 21, 1959

1. Name of Investigator: John P. Wyatt, M.D.
2. Title: Professor of Pathology
3. Institution St. Louis University School of Medicine  
& Address: 1402 S. Grand Boulevard, St. Louis 4, Missouri
4. Project or Subject: An Investigation into the Nature of the Pigmentary Lesion in Centrilobular Emphysema.
5. Detailed Plan of Procedure:

Utilizing the whole lung paper section technic<sup>1</sup> stereoscopic and histologic methods, a current morphologic analysis has revealed a distinctive anatomic form of emphysema, characterized by its early lesions developing in the central lobular portion of Miller's secondary lobule.<sup>2</sup> This distinctive form of emphysema is readily separated from the traditional obstructive vesicular emphysema with the lesion being at the respiratory bronchiole of orders 1 and 2.<sup>3,4</sup>

From our analysis to date, an outstanding structural change, associated with this respiratory bronchiolar lesion in centrilobular emphysema has been remarkable accumulation of black pigment. Although this black pigment is probably of exogenic derivation, studies of a definitive nature, concerning the origin, chemical and physical makeup, and the possible morphogenetic role of this pigment in centrilobular emphysema have not been undertaken previously.

It is our proposal, with micro-thin whole lung preparations and stereoscopy as aids in the identification and orientation of the respiratory bronchioles, to investigate more closely with precise micro dissection the physical and chemical nature of this "pigmentary" lesion by micro-incineration, volatility, fluorescence, and chromatographic studies.

As a complementary procedure to this physical and chemical analysis of the altered respiratory bronchioles, it is proposed with serial histologic sections to investigate in human tissues the existence and histologic makeup of the "sump pumps"<sup>5</sup> which apparently have their localization, anatomic and functional, at the 1st and 2nd respiratory bronchioles, the anatomic site of centrilobular emphysema. With this approach further insight into the neglected problem of the lung toilet and dust disposal may be gained.

6. Budget Plan:

Salaries	5,400.00
Expendable Supplies	920.00
Permanent Equipment	370.00
Overhead (15%)	1,003.00
Total	\$7,693.00 p.a.

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7. Anticipated Duration of Work: 2 years

8. Facilities and Staff Available:

Complete Pathologic Laboratory, including: Macro-section microtome (Wentworth type); Histochemical Laboratory, Fluorescent microscopy, Chemical Laboratory for Mineralogical Study; Chromatographic and Electrophoretic Apparatus.

Full-time Ph.D. Biochemist in Department of Pathology, as consultant to this project.

9. Additional Requirements:

Contemplate 2 additional technicians, one in morphology, one in biochemistry.

10. Additional Information:

Functional and Pathological Correlatives of Emphysema presently being supported by U.S.P.H.S. Grant. This grant H-3535 is primarily concerned with quantitating emphysema and adaptive changes as observed at postmortem with clinical aspects of the disease.

Signature John P. Wyatt, M.D.  
Director of Project

James W. Colbert Jr., M.D.  
Business Officer of Institution

#### References

1. Gough, J. The Use of Thin Sections of Entire Organs in Morbid Anatomical Studies. J. Roy. Micro. Soc., 69:231-235, 1949.
2. The Pathology of the Pneumoconiosis in Welsh Coal Miners. Proc. Int. Cong. in Ind. Med. Ed. 9. 661-667, 1948.
3. Wyatt, J. P. Macrosection and Injection Technics in Emphysema. 1st Internat. Conference at Aspen, Colorado, June 12-14, 1958. Published in July Issue of American Review of "Tuberculosis and Pulmonary Disease," July 1, 1959.
4. Centrilobular Emphysema. American Association of Pathologists and Bacteriologists, April 23, 1958, Boston, Mass.
5. Macklin, Charles. Pulmonary Sumps, Dust Accumulations, Alveolar Fluid and Lymph Vessels, Acta Anatomica, 23:1-33, 1955.

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